# **Transforming IVF**





# Disclaimer

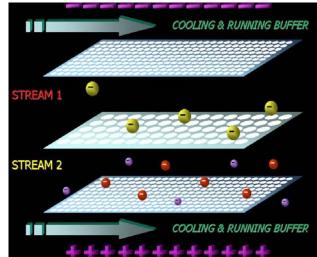
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# NuSep's technology selects high value proteins & cells based on size and charge

- NuSep (ASX: NSP) separates high value proteins and cells from fluids
- We use proprietary membranes (for size separation) and an electric field (for charge separation)
- We can separate proteins from blood serum\* and the best sperm from a semen sample
- NuSep has proven that its technology works and is now engaged in commercialising applications.

\* Performed through our majority owned investment, PrIME Biologics Pte Ltd





# Why is NuSep Technology Unique?

To our knowledge, no other company has

- a **proven proprietary** method for separating cells, viruses and proteins
- using a **membrane platform technology** that can precisely control pore size (for size separation)
- that can be combine with **electrophoresis technology** (for charge separation)
- in a way that can be scaled up to provide **commercial quantities** of product.

### NuSep has technological advantages across multiple applications

Application	Current	NuSep	o's Tec	hnolog	ical Advantages
	Methodology	Cheap er	Faster	Easier	Other
IVF (human & animal)	Density gradient centrifugation (DGC)	✓	~	~	<ul><li>Less damage to sperm</li><li>Extracts 'best' sperm</li></ul>
Plasma fractionation	Concentration/ fractionation	~	~		<ul> <li>More flexible: can process 10 – 10,000 litres.</li> </ul>
Recombinant protein purification	+ chromatography	✓	~		<ul> <li>Higher yield &amp; purity, hence less chromatography steps required</li> </ul>

### **NuSep has multiple separation systems**



BF400



CS10



Pilot scale GF100

NuSep has developed multiple devices for specific separation applications



# **Current Program Status**

# **PrIME Biologics Pte Ltd, Singapore:** NuSep's autonomous, majority owned investment

- Is preparing to commercially produce albumin and immunoglobulins from human blood serum
- PrIME is focussed on the underserved Asian plasma market
- **SpermSep:** Nusep's most advanced internal program
  - Has established human IVF benefits & has produced successful human births
  - Is preparing for further trials in major IVF Australian centres to demonstrate additional benefits over present practices
  - Has trials underway in animal IVF and artificial insemination

#### **New Membranes:**

Additionally, NuSep is developing new membranes for other commercial opportunities.

### **PrIME Biologics Pte Ltd Update**

- Investment by Xeraya Capital Labuan, a Malaysian biotech-focussed venture capital fund and J P Capital, Singapore
- Valuation prior to initial external investment: SGD\$27m
- Current major shareholdings:

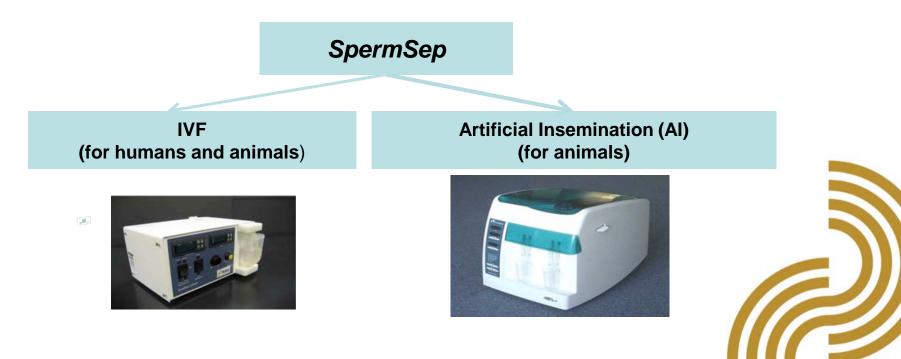
Shareholder	Share class	%	Investment to date (SGD \$m)
Xeraya & JP Capital	A (= control)	24.3	8.7
NuSep	B (non-voting)	72.6*	
Other (individuals)	B (non-voting)	3.1	

- Next major milestone, cGMP certification for the Singaporean production facility, anticipated by Q2 2015
- \* Based on completion of ~S\$2.7m investment by JP Capital under the S\$4m option agreement.

NB: NuSep's share would be diluted to 55% if Xeraya and JP Capital jointly invested to SGD\$19m, their maximum combined commitment on achievement of milestones by PrIME

## **SpermSep Addresses Male Infertility**

- NuSep's SpermSep devices select the healthiest, most viable sperm cells from semen samples quickly, cheaply, and with reduced sperm damage
- Current IVF processing is a multi-stage, expensive, hands-on process performed by lab technicians; SpermSep will provide the first dedicated sperm selection device for the IVF industry.



# Male Infertility is highly prevalent - and increases with age

- Male infertility is highly prevalent
  - is a factor in > 45% of infertile couples
  - ~5% of Australian men are infertile
- Has been increasing over the past few decades
- Fertility issues are more common in older men
  - Affects ~1/3 of men over 40
- There are also strong links between infertility and chronic disease eg cardiovascular disease, diabetes



#### Sperm quality, rather than quantity, is the issue

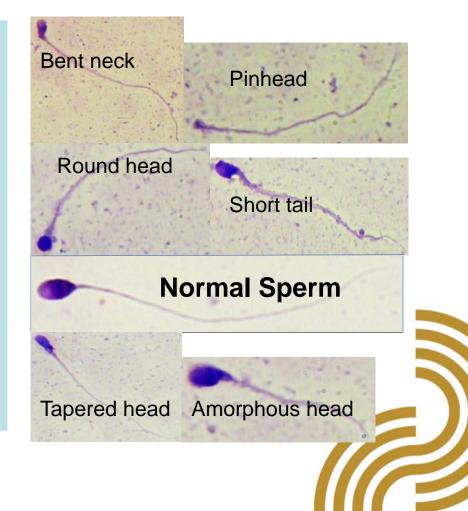
# A typical semen sample contains many abnormal sperm

- which the SpermSep process eliminates

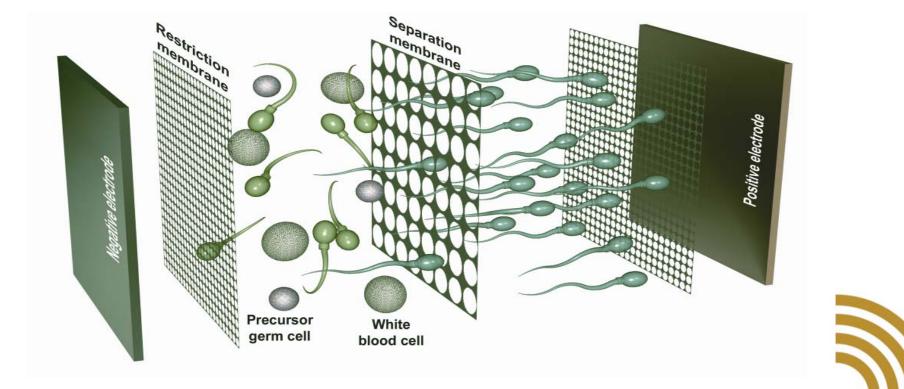
#### **Examples of sperm abnormalities:**

- double head or tail
- a short tail
- a tiny pinhead
- a bent neck
- a mis-shapen head eg round or tapered instead of oval
- damaged DNA

These factors affect their ability to move, to break the egg and/ or create a normal conception



# SpermSep works by separating the most viable sperm from semen samples



# Current sperm preparation methods have disadvantages

Density Gradient Centrifuge (DGC) method:

- Is the most common sperm preparation method used,
- It involves two damaging steps for sperm cells

2. <b>Culturing</b> Oxidative damage arises from the culture media - contains trace heavy metals, including copper	1. Centrifugation	Spinning creates damaging shear forces	<ul> <li>Increased risk:</li> <li>Infertility</li> <li>Premature birth/ birth defects</li> </ul>	
	2. Culturing	arises from the culture media - contains trace heavy metals,	disease & disability eg cancers, deafness, mental illness, metabolic	

# **Current artificial fertilisation processes (IVF** and ICSI) use DNA-damaged sperm from DGC

# Traditional IVF

(in vitro fertilisation)

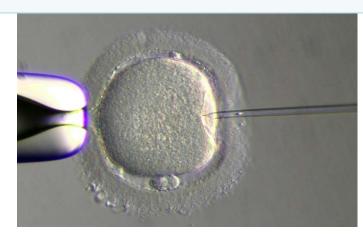
- Multiple sperm swim to the ovum.
- The first sperm to penetrate the ovum fertilises it.

#### ICSI

(intra cytoplasmic sperm injection)

- Used when male fertility is an issue.
- A single sperm is inserted into the ovum.
- Sperm is selected on appearance (morphology) and motility (ability to swim), not intact DNA.





# Spermsep has a commercial solution to key male infertility issues

#### Highly selective of healthy sperm

- The highly negatively charged sperm are the 'healthier'
- First to reach the (positive) anode through the separation membrane, leaving the less viable sperm behind

#### Far less damaging for sperm

 Sperm from our technology have significantly less DNA damage than from DGC method

# Cheaper, quicker, more convenient process

- Automated instrument
- disposable processing cartridges
- quick (5 mins/sample vs 40 mins/sample),
- much less manual lab tech time

Negatively charged head is attracted to anode

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# Small human IVF clinical trials completed - we have demonstrated proof of concept

- Prof John Aitken (Newcastle University) has published several papers in leading reproduction journals on the clinical benefits of SpermSep.
- These *in vitro* trials documented the improved sperm selection and reduced DNA-damage using the SpermSep method.
- Limited *in vivo* trials using SpermSep at Sydney IVF and Westmead Fertility Centre have demonstrated successful births
  - Couples had been unsuccessful with IVF
  - The trial showed there was no issue with safety, however the SpermSep machines now need to be upgraded to approved clinical devices.

# The Human IVF market is large and expanding

Couples with fertility issues: ~50m				
Global IVF clinic busines	Global IVF clinic business:			
Cycles/year	~15 m			
IVF babies/year	~350,000			
Numbers of IVF clinics	~3,000	EU is largest market Asia is fastest growing		
<b>IVF market size:</b> - 2012 - 2020 (forecast) - Australia	US\$ 9.3 b US \$21.6 b AUD\$470 m	Dominated by 5-6 companies		
Cost to patient per cycle	~US\$1,500 to ~US\$30,000	India USA		

Sources; Vitrolife 2013 Annual Report, Cooper/Origio investor Report, Jun 2012

# Human IVF consumable market is significantly smaller - but still substantial

	)
	Market size
	Industry growth rate
SD	
	Consumables cost/ IV (global average)
0 Sj	SpermSep Prices, Ma
	<ul> <li>Device price is antic customer commits t</li> </ul>
	<ul> <li>Single-use sterile S anticipated to be \$7</li> </ul>

Market size	US \$450 million pa
Industry growth rate	12% pa
	Driven by expansion in emerging markets, especially China
Consumables cost/ IVF cycle (global average)	~US \$300

#### argins

- cipated to be ~\$15,000, though free of charge if to long term consumables supply contract.
- permSep consumable pack price for human IVF is 75-100.
- Product margins >75%.

Sources; Vitrolife 2013 Annual Report, Cooper/Origio investor Report, Jun 2012

# Animal artificial reproduction market is large

#### Artificial insemination\* (AI) dominates

- IVF is used for elite, high value animals; rapidly expanding as emerging countries improve herd genetics
- AI market:
  - USA
    - ~66% of the nation's dairy cows
    - 70-75% of commercial swine production
  - Europe
    - ~90% of pigs and dairy cows
  - Al in other species
    - Non-thoroughbred horses (AI is illegal with thoroughbreds for racing)
    - goats, camels, zoos, greyhounds, endangered species, etc

\*sperm directly inserted into uterus



# **SpermSep in Animal IVF**

IVF is used for elite, high value animals

- Although still a niche market, it is rapidly expanding to improve herd genetics
  - eg IVF is being used by Shanghai Dairy (4<sup>th</sup> largest in China) to assist in growing the number of elite milking cows from 60,000 to 230,000 over the next 5 years
- NuSep is trialling bovine IVF (with Minitube Germany), and general animal reproduction in horses\* (with Uni. Newcastle) and sheep (with Uni. Sydney)







\*Artificial reproduction is banned in thoroughbred horses but can be used in other horses

# **SpermSep Clinical Trial Programs**

#### Human IVF

- Multi-centre *in-vitro* clinical trial at 4 leading IVF centres in Australia
- Aims to broaden validated IVF indications by testing on key categories of male infertility
- Begins Mar15, expected completion by Sept.



#### Animal IVF (and subsequently AI)

- Successful results to date from *in vitro* trials at Uni Newcastle (horses) and Uni Sydney (sheep)
- IVF bovine trials at Ludwig Maxmillian University (Munich) to commence in Q1'15.



Estimated cost to SpermSep business cash flow breakeven: ~A\$6 million.

# Competitors

SpermSep's competitor - in both human and animal IVF - is the DGC technique.

DGC uses standard lab centrifuges, plus consumables

SpermSep will be the first dedicated system for preparing sperm samples for artificial reproduction.

#### The major equipment & consumables suppliers:

- Human (Jun 2012):
  - Origio/Cooper 32%, Vitrolife (23%), Cook (16%), Irvine (11%) Sage/Cooper (7%).
- Animal:
  - The global market leader is Minitube (Germany), NuSep's SpermSep distributor



### **IP, Patents, Protection**

-or personal use

NuSep has patents and know how on its core separation IP and the SpermSep application.

NuSep has a license to all the Prime Biologics IP for use in fields outside human plasma separation.

# The University of Newcastle (UN) has licensed to NuSep its patents and IP on the SpermSep application

- Key UN patent is granted in Australia, USA, UK and Germany
- UN will receive a small royalty on SpermSep sales
- UN is also engaged in ongoing funded research with NuSep in the assisted reproduction field



# NuSep's Board

	Qualifications	Experience
Alison Coutts (Exec Chairman)	B.E (Chem), MBA, Grad Dip Biotech	Engineering project management, strategy consulting, executive search, financial services and capital markets, technology commercialisation, governance, listed board & senior management experience
Andrew Goodall (Non-Exec director)		International commercial property management, founding and management of successful small business. Major shareholder.
Michael Graham (Non-Exec director)	B.A, Dip Mgt	Company secretarial, global marketing communications, governance, technology commercialisation, founding and management of high tech start up, experienced board member
Mark Gell (Non-Exec director)	B.Ec, MBA, Member AICD	Capital markets, investor relations and senior management within large corporates, consulting, commercialisation of new ventures, governance, experienced board member

# **NuSep Shareholding Structure**

Number of shares on issue	237,606,002	NSP - Daly Line Chart [Close]
Past 6 month share price range	4.3 – 8.0 cents	
Market Capitalisation	\$19 million (@8.0 cents/shr) \$15.4 million (@6.5 cents/shr)	NSP - Volume         300000
No. of shareholders	941	
Top holdings	<ul> <li>Top : 38.9%*</li> <li>Top 5: 45.7%%</li> </ul>	
*Goodall & related p	arties	

# **NuSep Key Financials**

#### The balance sheet has improved post the 19 Dec'14 AGM

- Over \$4 million in debt has been converted to equity
- The Net Asset position is now positive at ~\$2 million
- Current Assets also now exceed Current Liabilities by \$0.45 million
- The main liability, \$4.4 million, is the debt on PrIME's Singapore production facility, which NuSep agreed to adopt as part of the agreement to spin out PrIME
  - This debt is repayable starting in March 2016 and is required to be paid for NuSep to maintain its investment in PrIME

#### Cash on hand end Jan: ~\$400K

#### Cash burn per month:

- \$150K min;
- \$260K pm max (with all growth programs covered)



# Funding Requirement – 2015

Use of Funds		\$'000
Product Development		
	Commercial IVF system	\$700
	Membranes	\$230
SpermSep Clinical Trials		\$220
Market Development		\$300
Corporate		\$800
Working capital		\$150
		\$2,400

Additional operational funding required 2016 & 2017: \$3.9m (excludes debt repayment)

### **SpermSep Project Launch Milestones**

	F۱	FY15		FY16				FY17	
NUSEP - PROJECT MILESTONES & COSTS		4Q	1Q	2Q	3Q	4Q	1Q	2Q	
SPERMSEP									
To First   To First Revenues									
SpermSep commercial system devt (m/c, consuma	ables)								
Regulatory prep, filing & approval	CE								
	FDA								
Clinical Trials	Aust								
Internat	tional								
SpermSep Production set up and Production build									
First shipments Human IVF - rese	earch								
Human IVF - cli	nical								
Anin	nal AI								
MEMBRANES									
New Apps Development/Validation									
App A research, protoype, develop IP									
App B research, protoype, develop IP,									
App C research, protoype, develop IP,									

# Summary

# NuSep has unique proprietary technology in biological separations

- Proven to work
- Two major applications: human plasma (through investment in PrIME) and sperm separation
- Multiple unique benefits over incumbent technology

#### SpermSep

- Entering clinical trials, in human IVF and animal (initially IVF)
- Large fast-growing global market
- International distribution partnership in place for animal fertility

#### **Further Capital Required for**

- Funding of multi-centre clinical trials
- Development and market launch of production SpermSep system
- Development of new membranes